

IN THE SPECIFICATION

Please amend the specification as shown in the following marked up version of the original paragraph:

The paragraph beginning on Page 1, line 13 is amended as follows:

In normal tissues, cellular connective tissue synthesis is offset by extracellular matrix degradation, the two opposing effects existing in dynamic equilibrium. Degradation of the matrix is brought about by the action of matrix metalloproteinases (MMPs) released from resident connective tissue cells and invading inflammatory cells. Normally, these catabolic enzymes are tightly regulated at the level of their synthesis and secretion and also at the level of their extracellular activity. Extracellular control occurs primarily by regulation with specific enzymes, such as TIMPs (tissue inhibitors of metalloproteinases), which form complexes with MMPs. These complexes prevent MMP action. Cellular level control of MMP activity occurs primarily by regulating MMP gene expression and [[y]] down regulating the expression of the membrane bound MMPs (MT-MMP) that activate the excreted proenzyme form of the MMP.

The paragraph beginning on Page 4, line 10 is amended as follows:

Given the large number of diseases associated with MMP activity, there is a need to control MMP activity. Several approaches have been suggested to accomplish such regulation. One approach has focused on the catalytic role of zinc in MMPs, and designing zinc chelating

regulators. Potent regulators have been generated by introducing zinc chelating groups, such as peptide hydroxamates and thiol-containing peptides, into substrates. Peptide hydroxamates and TIMPs have been successfully used in animal models to treat cancer and inflammation. While these hydroxamates are potent ~~[[at]]~~ as regulators of MMPs by binding to zinc, they are toxic to humans because they bind to all zinc-containing enzymes. Because many biochemical reactions occurring in the body require zinc, use of the hydroxamates detrimentally effects these other functions and can result in death.

The paragraph beginning on Page 7, line 11 is amended as follows:

Furthermore, there is a need in the art for MMP inhibitors that are not toxic to the individual to whom they are ~~adminisered~~ administered.

The paragraph beginning on Page 8, line 8 is amended as follows:

In another aspect, the present invention provides a method for making the new class of MMP regulators. The method comprises binding a zinc chelator to synthetic peptides. The peptide sequences chosen were the part of the TIMP that made the closest approach to the MMP ~~[[n]]~~ in the vicinity of the catalytic zinc. The sequence is a common structural feature of the binding interface.